Investigation of Chinese Herbal Medicine in treatment of Metabolic Syndrome

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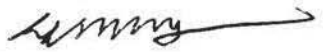
Declaration

I declare that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree except as fully acknowledged within the text. I also declare that this thesis has been written by me. Any help I received in my research and preparation of this thesis has been acknowledged.

Signature of Student



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Communications

Parts of this thesis have already been presented in abstract form at a scientific meeting:

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Kim, J. J. Y., Tan, Y., Shim, J. H. B., Kim, C. H. J. & Qu, X. (2008) The Effects and Mechanisms of Notoginsenosides on Glucose and Lipid Metabolism in 3T3-L1 Cells. Annual Scientific Meeting of Australian Diabetes Society (ADS) Melbourne, Australia.

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List of Abbreviations

ASCVD	Atherosclerotic cardiovascular disease
AUC	Area under curve
FFA	Free fatty acids
GLUT-4	Glucose transporter-4
HDL-C	High density lipoprotein cholesterol
HFD	High fat diet
IDF	International Diabetes Federation
i.p. GTT	Intra-peritoneal glucose tolerance test
i.p. ITT	Intra-peritoneal insulin tolerance test
LDL-C	Low density lipoprotein cholesterol
MetS	Metabolic syndrome
NCEP	National Cholesterol Education Program
NEFA	Non-esterified fatty acids
PI(3)k	Phosphatidylinositol 3-kinase
PPAR	Peroxisome proliferator-activated receptor
RAAS	Renin-angiotensin-aldosterone-system
SEM	Standard error of mean
STZ	Streptozotocin
T2DM	Type 2 diabetes mellitus
TNF-α	Tumour necrosis factor-α
TZD	Thiazolidinedione
VLDL-C	Very low density lipoprotein cholesterol
WHO	World Health Organisation

Abstract

Metabolic syndrome (MetS) is a clustering of atherosclerotic cardiovascular disease (ASCVD) risk factors including central obesity, insulin resistance, dyslipidaemia, hypertension, and pro-inflammatory and pro-thrombotic states. It is also a precursor of type 2 diabetes mellitus (T2DM). Research continues to uncover the mechanical links of the pathogenesis of MetS as well as to discover new drugs to target the multiple metabolic and haemodynamic abnormalities of MetS. The focus of this thesis is on the investigation of two Chinese herbal medicines, Sugarid and SK0504, in the treatment of MetS and T2DM induced in C57BL/6J mice by high fat diet (HFD) feeding with or without streptozotocin (STZ) injection.

The results described in Chapter 3 show that T2DM was induced in mice fed HFD when their blood glucose levels rose after the STZ injection. Treatment with a Chinese herbal product, Sugarid did not show any significant improvements of body and visceral fat weights, glucose metabolism, insulin sensitivity, and serum and liver lipid parameters in either MetS and T2DM models of mice. Therefore, the findings from this study do not support the notion of Sugarid being a potential drug in treatment of MetS and T2DM.

The purpose of Chapter 4 is to investigate the effects and mechanisms of a new herbal formula, SK0504 in HFD fed mice. Treatment with SK0504 showed significant improvements of visceral fat weight, insulin sensitivity and some biochemical parameters. The findings of this study showed potential beneficial effects of SK0504 on MetS by its ability to target central obesity, insulin resistance and hyperlipidaemia. However, the hypothesised effects of SK0504 in targeting the multiple metabolic

abnormalities of MetS were not obtained. The last chapter outlines possible avenues for further research in order to confirm any implications of the experimental findings reported in this thesis.